

PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

29 FEB. 1996 PCT

To:

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**NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

(PCT Rule 71.1)

Date of mailing
(day/month/year)

29.02.96

Applicant's or agent's file reference
4150 PC 1

IMPORTANT NOTIFICATION

International application No.

PCT/DK 95/00080

International filing date (day/month/year)

23/02/1995

Priority date (day/month/year)

23/02/1994

Applicant

BM RESEARCH A/S et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

29 FEB. 1996


REV

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Applicant's or agent's file reference 4150 PC 1		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/DK 95/ 00080	International filing date (day/month/year) 23/02/1995	Priority date (day/month/year) 23/02/1994	
International Patent Classification (IPC) or national classification and IPC A61K9/22			
Applicant BM RESEARCH A/S et al.			

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets, including this cover sheet.
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
These annexes consists of a total of 2 sheets.

- This report contains indications and corresponding pages relating to the following items:
 - ☒ Basis of the report
 - ☐ Priority
 - ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - ☐ Lack of unity of invention
 - ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain documents cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application

Date of submission of the demand 19/09/1995	Date of completion of this report 29.02.96
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer A. Amaro Telephone No. 8635

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.
PCT/DK95/00080

I. Basis of the report

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

☐ the international application as originally filed.

☒ the description, pages 1-20 _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. 1-27 _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 28-33 _____, filed with the letter of 22.01.96,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____.

☐ the claims, Nos. _____.

☐ the drawings, sheets/fig _____.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORTIntern. application No.
PCT/DK95/00080

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-33 _____	YES
	Claims _____	NO
Inventive Step (IS)	Claims 1-33 _____	YES
	Claims _____	NO
Industrial Applicability (IA)	Claims 1-33 _____	YES
	Claims _____	NO

2. CITATIONS AND EXPLANATIONS

1. Having regard to the documents cited in the international search report, the subject-matter of claims 1-33, is considered as being novel according to Article 33 (2) PCT, as a composition for controlled delivery comprising a matrix and a coating and the method to produce said composition, as defined in said claims 1-33, has not been described in any of the cited documents.
2. It is known to obtain sustained release of an active substance by embedding it in a matrix of an insoluble substance from which the active substance will gradually diffuse. Furthermore, from WO-89/09066 and WO-91/04015 (same Applicant as the present invention) are known controlled release compositions containing a matrix of a crystalline PEG polymer with a non-ionic emulsifier dispersed therein, and an active substance dispersed either throughout the matrix or in certain zones within the matrix. When the inventors faced the problem of providing these compositions with a slowly erodible coating that

can function in a manner complementary to the controlled erosion of the matrix containing the active substance (p.2, l. 30-34 + p.3, l.1-2), they solved by the composition, subject-matter of claim 1, and the method to produce said composition (claim 28). As this solution, providing erosion of the matrix and release of the active substance only from the surface or surfaces that are not covering by the coating, is neither disclosed nor suggested in any of the documents cited in the international search report, it is considered to meet the requirements of Article 33 (3) PCT regarding inventive step.

3. The claimed invention (claims 1-33) is considered industrially applicable (Article 33 (4) PCT) as the claimed compositions should be manufactured in the industry.

28. A method for producing a composition for controlled
5 delivery of at least one active substance into an aqueous
medium by erosion at a preprogrammed rate of at least one
surface of the composition, the method comprising forming, by
means that include extrusion or injection moulding,
i) a matrix comprising the active substance, the matrix
10 being erodible in the aqueous medium in which the
composition is to be used, and
ii) a coating having at least one opening exposing at
least one surface of said matrix, the coating
comprising
15 a) a first cellulose derivative which has thermoplastic
properties and which is substantially insoluble in
the aqueous medium in which the composition is to be
used,
and at least one of
20 b) a second cellulose derivative which is soluble or
dispersible in water,
c) a plasticizer, and
d) a filler,
said coating being a coating which crumbles and/or erodes
25 upon exposure to the aqueous medium, in particular a body
fluid, at a rate which is equal to or slower than the rate at
which the matrix erodes in the aqueous medium, allowing
exposure of said surface of the matrix to the aqueous medium
to be controlled.
- 30 29. A method according to claim 28 wherein the composition is
produced by co-extrusion of a) the matrix material with the
active substance dispersed therein and b) the coating.
30. A method according to claim 28 wherein the composition is
produced by injection moulding of the coating and subsequent

AMENDED SHEET

injection moulding of the matrix containing the active substance.

31. A method according to claim 28 wherein the composition is produced by injection moulding of the coating and subsequent
5 injection moulding of alternating layers comprising at least one layer comprising matrix material and at least one layer comprising the active substance.

32. A method according to claim 28 wherein the composition is produced by injection moulding of the matrix containing the
10 active substance, or injection moulding of alternating layers comprising at least one layer comprising matrix material and at least one layer comprising the active substance, into a pre-formed tube which forms the coating.

33. A method according to claim 28 wherein the composition is
15 formed by extrusion or injection moulding of the matrix containing the active substance followed by dip coating.

AMENDED SHEET